

Nocturnal Temazepam in the Treatment of Narcolepsy

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Narcolepsy is characterized by fragmented nighttime sleep and frequent arousals. One treatment approach to improve daytime symptoms is to consolidate nighttime sleep through decreasing arousals. Sodium oxybate is the first FDA-approved medication that follows this approach. Benzodiazepines are known to also decrease arousals at night and have been proposed to help with sleep fragmentation. In one report, clonazepam was shown to improve cataplexy in 10 of 14 patients with narcolepsy although

no improvement in daytime sleepiness was reported. The purpose of this case review was to share our experience of nocturnal temazepam on daytime sleepiness in patients with narcolepsy as measured by the Epworth Sleepiness Scale (ESS).

Keywords: Narcolepsy, temazepam

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Narcolepsy is characterized by fragmented nighttime sleep and frequent arousals. One treatment approach to improve daytime symptoms is to consolidate nighttime sleep through decreasing arousals. Sodium oxybate is the first FDA-approved medication that follows this approach. Benzodiazepines are known to also decrease arousals at night and have been proposed to help with sleep fragmentation.¹ In one report, clonazepam was shown to improve cataplexy in 10 of 14 patients with narcolepsy although no improvement in daytime sleepiness was reported.² The purpose of this case review was to share our experience of nocturnal temazepam on daytime sleepiness in patients with narcolepsy as measured by the Epworth Sleepiness Scale (ESS).

REPORT OF CASES

In this retrospective case series, the records of patients diagnosed with narcolepsy and treated with temazepam were examined. Diagnosis was based on a combination of polysomnography, multiple sleep latency testing, and clinical presentation in accordance with the diagnostic criteria from the International Classification of Sleep Disorders, 2nd edition.³ All 7 patients had a history of cataplexy, but only 5 had ongoing attacks more often than once a month. Doses of temazepam ranged from 15 mg to 30 mg and were administered once nightly prior to bedtime for a minimum of one week. All other medications and doses were unchanged during the temazepam titration. Each patient had a quantified measure of daytime sleepiness through the ESS both prior to initiation of temazepam and at each tolerated dose. Baseline ESS and ESS at the highest tolerated temazepam dose were compared using a paired sample t-test. Seven patients were included in this review. The age of patients ranged from 9 to 71 years, with a mean age of 35 years. They were diagnosed with narcolepsy for a mean of 14 years (range 1 to 49 years). Six patients reported a decrease in daytime sleepiness on temazepam, with a mean change in ESS score of -5.1 points (range -10 to 1, see **Figure 1**). The mean ESS score was 16.4 prior to initiation of

temazepam and was 11.3 on the highest tolerated dose. This difference was statistically significant ($p = 0.007$). Although not quantified, four patients who had frequent cataplexy at the time of initiation of temazepam reported a subjective improvement in frequency of cataplexy, three of whom had improvement in their subjective sleepiness. Six of the 7 patients elected to remain on the temazepam. See **Table 1** for further information on sleep characteristics of individual patients.

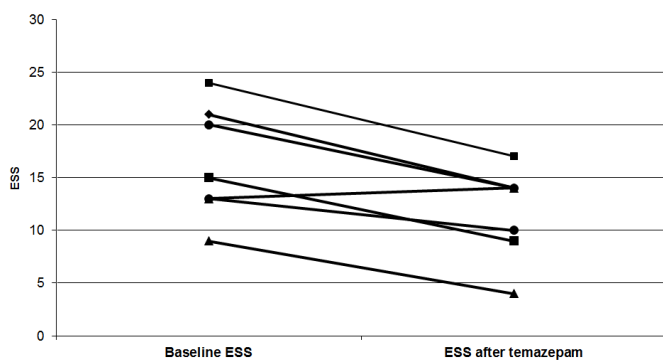
DISCUSSION

Nocturnal temazepam may be an option to improve excessive daytime sleepiness in patients with narcolepsy. Based on our experience, temazepam appears to improve subjective sleepiness as measured by ESS scores and anecdotally improves the frequency of cataplexy. Narcolepsy patients are known to have fragmented sleep and frequent sleep stage shifts. Therapeutic guidelines recommend sodium oxybate as a treatment option for cataplexy. Large clinical trials suggest benefit to excessive daytime sleepiness and cataplexy may in part be mediated by the drug's ability to consolidate sleep.^{4,5} Temazepam may have a similar action in patients with narcolepsy by consolidating sleep. Unlike sodium oxybate, temazepam is not known to increase slow wave sleep.^{6,7} Our study is limited by the retrospective approach and the small sample size. The population is mixed, including both pediatric and adult patients, as well as patients with and without cataplexy. We also did not perform polysomnography immediately prior to and following temazepam use and therefore do not have data to further speculate regarding the mechanism. Finally, we used the ESS as a measure of daytime sleepiness as opposed to the more objective MSLT. One prior study using triazolam showed no change in MSLT, which emphasizes the importance of objective measures for sleepiness.⁸ However, triazolam is also a short-acting agent, so might not work as well as temazepam.

Of note, the five adult patients in our study had a mean decrease in ESS score of 7 points. Our two pediatric patients

Table 1—Sleep characteristics for individual patients

Patient	Subjective sleep quality off Temazepam	Age	Gender	Spontaneously reported improvement in cataplexy	ESS baseline	ESS on 7.5mg temazepam	ESS on 15 mg temazepam	ESS on 30 mg temazepam
1	Poor	71	F		21	N/A	13.5	14
2	Poor	37	F	Yes	20	N/A	15	14
3	Mildly disturbed	38	F		9	5	4	N/A
4	Mildly disturbed	18	M	Yes	15	N/A	Not recorded	9
5	Mildly disturbed	9	F	Yes	13	Not recorded	14	N/A
6	Brief awakenings	14	F		13	N/A	10	N/A
7	Poor	57	F	Yes	24	N/A	17	14

Figure 1—Individual changes in ESS with temazepam

had a mean decrease of only 1 point. One of these patients had an increase in ESS. Given the fact that adults with narcolepsy have more arousals from sleep than children, this difference in response to temazepam would be expected if the improvement in daytime functioning is a result of increased sleep consolidation. Interestingly, one pediatric patient did report improvement in frequency of cataplexy. Although temazepam may be an option in the future treatment of narcolepsy patients, further prospective, placebo-controlled trials are needed to establish the effectiveness of temazepam therapy in both children and adults.

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